

UNCLASSIFIED

SECURITY CLASSIFICATION OF THIS PAGE (When Data Entered)

UTIL FILE COPY

(4)

REPORT DOCUMENTATION PAGE

READ INSTRUCTIONS
BEFORE COMPLETING FORM

1. REPORT NUMBER

2. GOVT ACCESSION NO.

3. RECIPIENT'S CATALOG NUMBER

4. TITLE (and Subtitle)

Cardiac Isoenzyme Values after Total Joint
Arthroplasty Number 240: March 1989

5. TYPE OF REPORT & PERIOD COVERED

6. PERFORMING ORG. REPORT NUMBER

AUTHOR(s)

Dane Wukich and GM Graeber

8. CONTRACT OR GRANT NUMBER(s)

PERFORMING ORGANIZATION NAME AND ADDRESS
Division of SurgeryWalter Reed Army Institute of Research
Washington, DC 20307-51-010. PROGRAM ELEMENT, PROJECT, TASK
AREA & WORK UNIT NUMBERS

CONTROLLING OFFICE NAME AND ADDRESS

US Army Research and Development Command
Fort Detrick, Frederick, MD 21701

12. REPORT DATE

13. NUMBER OF PAGES

11. MONITORING AGENCY NAME & ADDRESS (if different from Controlling Office)

Walter Reed Army Institute of Research
Washington, D.C. 20307-5100

15. SECURITY CLASS. (of this report)

15a. DECLASSIFICATION/DOWNGRADING
SCHEDULE

16. DISTRIBUTION STATEMENT (of this Report)

Approved for public release; distribution unlimited

17. DISTRIBUTION STATEMENT (of the abstract entered in Block 20, if different from Report)

18. SUPPLEMENTARY NOTES

19. KEY WORDS (Continue on reverse side if necessary and identify by block number)

20. ABSTRACT (Continue on reverse side if necessary and identify by block number)

Accession For

NTIS GRA&I

DTIC TAB

Unannounced

Justification

By

Distribution/

Availability Codes

Dist

Avail and/or
Special

A-120

DD FORM 1 JAN 78 1073

EDITION OF 1 NOV 65 IS OBSOLETE

SECURITY CLASSIFICATION OF THIS PAGE (When Data Entered)

- J. R. III, Mazza, J. J., Larson, D. E., Chen, H. M., Milbauer, J. P., Treuhart, P. S., Plotka, E. D., Wenzel, F. J., Nycz, G., and Pierce, W. E.: Aspirin-sulfinpyrazone in prophylaxis of deep venous thrombosis in total hip replacement. *JAMA* 250:2649, 1983.
108. Schondorf, T. H., and Hey, D.: Combined administration of low dose heparin and aspirin as prophylaxis of deep venous thrombosis after hip joint surgery. *Haemostasis* 5:20, 1976.
109. Schondorf, T. H., and Weber, U.: Prevention of deep vein thrombosis in orthopedic surgery with the combination of low dose heparin plus either dihydroergotamine or dextran. *Scand. J. Haematol.* 25:126, 1980.
110. Schwarz, H. P., Fischer, M., Hapmeyer, P., Batard, M. A., and Griffin, J. H.: Plasma protein S deficiency in familial thrombotic disease. *Blood* 6:1297, 1984.
111. Sevitt, S., and Gallagher, N. G.: Prevention of venous thrombosis and pulmonary embolism in injured patients: Trial of anticoagulant prophylaxis with phenindione in middle-aged and elderly patients with fractured necks of femur. *Lancet* 2:981, 1959.
112. Shepard, R. M., White, H. A., and Shirkey, A. L.: Anticoagulant prophylaxis of thromboembolism in post-surgical patients. *Am. J. Surg.* 112:692, 1966.
113. Sie, P., Pichon, J., Dupony, D., and Bonen, B.: Constitutional heparin cofactor II deficiency associated with recurrent thrombosis. *Lancet* 2:414, 1985.
114. Sigel, B., Felix, W. R., Pepky, G. L., and Ipsen, J.: Diagnosis of lower limb venous thrombosis by Doppler ultrasound technique. *Arch. Surg.* 104:174, 1972.
115. Skinner, D. B., and Salzman, E. W.: Anticoagulant prophylaxis in surgical patients. *Surg. Gynecol. Obstet.* 125:741, 1967.
116. Smyrnis, S. A., Kolios, A. S., and Aguantis, J. K.: Deep-vein thrombosis in patients with fracture of the upper part of the femur: A phlebographic study. *Br. J. Surg.* 60:447, 1973.
117. Soreff, J., Johnsson, H., Diener, L., and Goransson, L.: Acetylsalicylic acid in a trial to diminish thromboembolic complications after elective hip surgery. *Acta Orthop. Scand.* 46:246, 1975.
118. Sproule, E. E.: Carcinoma and venous thrombosis: The frequency of association of carcinoma in the body or tail of the pancreas with multiple venous thromboses. *Am. J. Cancer* 34:566, 1938.
119. Stamatakis, J. D., Kakkar, V. V., Sagar, S., Lawrence, D., Nairn, D., and Bentley, P. G.: Femoral vein thrombosis and total hip replacement. *Br. Med. J.* 2:223, 1977.
120. Stead, N. W., Bauer, K. A., and Kinney, T. R.: Venous thrombosis in a family with defective release of vascular plasminogen activator and elevated plasma factor VIII/von Willebrand factor. *Am. J. Med.* 74:33, 1983.
121. Stevens, J., Fardin, R., and Frenck, R. J.: Lower extremity thrombophlebitis in patients with femoral neck fractures: A venographic investigation and a review of the early and late significance of the findings. *J. Trauma* 8:527, 1968.
122. Strandness, D. E.: Thrombosis detection by ultrasound, plethysmography, and phlebography. *Semin. Nucl. Med.* 7:215, 1977.
123. Stulberg, B. N., Dorr, L. D., Ranawat, C. S., and Schneider, R.: Aspirin prophylaxis for pulmonary embolism following total hip arthroplasty. An incidence study. *Clin. Orthop.* 168:119, 1982.
124. Tran, T. H., Marlet, G. A., and Duckert, F.: Association of hereditary heparin cofactor II deficiency with thrombosis. *Lancet* 2:413, 1985.
125. Trousseau, A.: Phlegmasia Alba Dolens. *Clinique Medicale de l'Hotel-Dieu de Paris, London. New Sydenham Society* 3:94, 1965.
126. Turpie, A. G. G., Levine, M. N., Hirsch, J., Carter, C. J., Jay, R. M., Powers, P. J., Andrew, M., Hull, R. D., and Gent, M.: A randomized controlled trial of low-molecular-weight heparin (enoxaprin) to prevent deep-vein thrombosis in patients undergoing elective hip surgery. *New Engl. J. Med.* 315:925, 1986.
127. Users Reminded About Adverse Reactions to Dextran. *FDA Drug Bulletin* 13:23, 1983.
128. Vessey, M. P.: Female hormones and vascular disease: Epidemiologic overview. *Br. J. Fam. Plan.* 6:1, 1980.
129. Virchow, R.: *Thrombose und Embolie (1846-1856)*. Leipzig, East Germany, Verlag-von Johann Ambrosius Barth, 1910.
130. Walenga, J. M., Fareed, J., and Hoppensteadt, D. A.: In vitro coagulant and amidolytic methods for evaluating the activity of heparin and a low molecular weight derivative (PK 10169P). *Semin. Thromb. Hemost.* 11:17, 1985.
131. Westermann, K., Trentz, O., Pretschner, P., and Mellman, A.: Thromboembolism after hip surgery. *Int. Orthop.* 4:253, 1981.
132. Wheeler, H. L., O'Donnell, J. A., and Anderson, F. A.: Bedside screening for venous thrombosis using occlusive impedance phlebography. *Angiology* 26:199, 1975.
133. Winter, J. H., Fenech, A., and Ridley, W.: Familial antithrombin III deficiency. *Q. J. Med.* 51:373, 1982.
134. Wood, W. H., Prentice, C. R. M., and McNicol, G. P.: Association of fibrinogen-fibrin-related antigen (F. R.-antigen) with postoperative deep-vein thrombosis and systematic complications. *Lancet* 1:166, 1972.
135. Zekert, F.: *Thrombosen Embolien und Aggregationshemmer in der Chirurgie*. Stuttgart, Germany, Schattner, 1975.

Cardiac Isoenzyme Values After Total Joint Arthroplasty

DANE K. WUKICH, MAJ, MC, JOHN J. CALLAGHAN, MAJ, MC,
GEOFFREY M. GRAEBER, LTC(P), MC, THOMAS MARTYAK, MAJ, MC,
CARLTON G. SAVORY, COL, MC, AND SP/4 JONATHAN J. LYON

→ The purpose of this study was to prospectively determine what effect total joint arthroplasty had on the myocardial-associated isoenzymes of serum creatine kinase (CK-MB) and lactate dehydrogenase (LD-1:LD-2). Fifty patients treated with total joint arthroplasty of the hip or knee had isoenzyme determinations using automated spectrophotometry and agarose gel electrophoresis. Skeletal muscle injury associated with the trauma of surgery resulted in significant elevations of the absolute value of CK-MB; however, the percentage of CK-MB comprising total CK activity and LD-1:LD-2 did not rise significantly in patients who did not experience postoperative myocardial infarction. It is important to determine both serum CK-MB and LD-1:LD-2 in suspected postoperative myocardial infarction since false positive elevations of CK-MB can occur. Elevations of CK-MB exceeding 50 International Units/liter or 5% of the total CK activity combined with LD-1:LD-2 exceeding 1.0 should not be attributed to skeletal muscle injury alone following total joint arthroplasty of the hip or knee. *Keywords:*

Surgery; Joint arthroplasty; Reprints; (K)

From Orthopaedic Surgery Service and Cardiology Service, Walter Reed Army Medical Center, The Division of Surgery, Walter Reed Army Institute of Research, Washington, D.C., and The Department of Surgery, The Uniformed Services University of the Health Sciences, Bethesda, Maryland.

The opinions and assertions contained herein are the private views of the authors and are not to be construed as official or as reflecting the views of the Department of the Army or the Department of Defense.

Reprint requests to Dane K. Wukich, M.D., Orthopaedic Surgery, Walter Reed Army Medical Center, Washington, D.C. 20307.

Received: February 17, 1988.

Perioperative cardiovascular complications following total joint arthroplasty of the hip or knee have been reported to occur in 0.5%–5.0% of patients.^{3–6,10,11,15,21,24,29,31–34} Since well over 100,000 total joint arthroplasties of the hip or knee are performed annually in the United States, the number of perioperative cardiovascular complications is significant.¹⁹ Recent studies of noncardiac surgical patients (including orthopedic patients) found that postoperative myocardial infarction was associated with a 25%–43% incidence of cardiac death.^{1,12} Therefore, early accurate diagnosis of perioperative myocardial infarction is paramount since the classic presentation may be masked by postoperative pain, medications, or noncardiac complications.

Serum lactic dehydrogenase (LD), creatine kinase (CK), and their isoenzymes are used routinely to diagnose acute myocardial infarction in nonsurgical patients.^{8,13,23} It is well known that surgical manipulation of skeletal muscle causes elevation of serum total LD and CK; however, the effect of total joint arthroplasty on these enzymes and their isoenzymes has not been studied in detail.^{2,9,16} The purpose of this prospective study was to determine what effect total joint arthroplasty of the hip or knee has on these enzymes in patients who have not experienced acute perioperative myocardial infarction.

89 9 20 014
140 05 232 68

MATERIALS AND METHODS

The protocol for this prospective study was approved by the Department of Clinical Investigation and the Human Use Committee at the authors' institution prior to obtaining any samples from patients. Fifty patients treated with total joint arthroplasty of the hip or knee were included in this study. Twenty-five patients ranging in age from 42 to 89 years were treated with 25 total hip arthroplasties, while 25 patients ranging in age from 41 to 81 years were treated with 27 total knee arthroplasties (two patients had staged bilateral total knee arthroplasties). All arthroplasties were primary except for one hip revision and one knee revision. All primary total hip arthroplasties were performed through a posterior approach, and the one total hip revision was performed through a transtrochanteric approach. All total knee arthroplasties were performed through a medial parapatellar approach that was extended proximally and distally.¹⁸ Twenty-three of the 50 patients (45%) were older than 70 years of age. All 52 joint arthroplasties were performed electively as either the first (approximate starting time, 9 AM) or second (approximate starting time, 12 noon) case of the day.

Each patient had 7 mm of peripheral venous blood drawn preoperatively and on postoperative Day 1 (15–18 hours postoperative), Day 2 (39–42 hours postoperative), and Day 3 (63–66 hours postoperative). All blood was drawn between 6 AM and 8 AM each day. These particular times were chosen because maximal elevations of serum CK occur within 24 hours following myocardial infarction, while maximum elevations of LD occur on Day 3 and later following infarction. The peak incidence of postoperative myocardial infarction occurs by postoperative Day 3.⁸ Total serum CK and LD were determined by automated spectrophotometry using the Encore Pipettor 2000 (Baker Instruments, Allentown, Pennsylvania). Only reagents and controls specific for use with this system were used for the analysis.^{22,27} Absolute values for total CK and LD were recorded in International Units/liter (IU/l). The serum isoenzymes of CK (CK-MM, CK-MB, CK-BB) and LD (LD-1 to LD-5) were determined by agarose gel electrophoresis using the Corning agarose clinical isoenzyme system (Corning, New York).^{17,26,30,35} Only Corning controls and reagents specific for this system were used in the analysis. The isoenzymes were recorded as the percentage of that particular isoenzyme comprising total enzyme activity. Absolute values in IU/l for each isoenzyme were then calculated by multi-

plying the total enzyme activity by the percentage of that particular isoenzyme. The specific methodology used in the authors' laboratory has recently been published.¹³ The ratio of LD-1 to LD-2 was also calculated on all samples since a value for this determination exceeding 1.0 suggests myocardial injury.^{9,13,23}

Each of the 50 patients had resting 12-lead electrocardiograms performed preoperatively and immediately postoperatively in the recovery room. All electrocardiograms were interpreted by one cardiologist who was unaware of the results of the enzyme studies. Acute perioperative myocardial infarction was diagnosed if there were classic electrocardiographic changes or if serum isoenzymes indicated myocardial injury.²⁸ For the purpose of this study, enzymatic diagnosis of myocardial infarction was defined by an absolute value of CK-MB exceeding 50 IU/l and LD-1:LD-2 greater than 1.0.^{13,14} These values have been used previously in studies of perioperative myocardial infarction in the authors' laboratory. Preoperative values were compared to postoperative values (preoperative *versus* postoperative Day 1 (POD1), preoperative *versus* POD2, and preoperative *versus* POD3) using the paired Student's *t*-test to determine statistical significance. Increases in total CK and total LD were compared to respective enzyme samples using the two-sample *t*-test to determine statistical significance.⁷

RESULTS

TOTAL HIP ARTHROPLASTY

There were 25 preoperative samples and 75 postoperative samples. The mean total serum LD was not significantly elevated postoperatively, although the elevations on POD1 suggest a difference (Tables 1 and 2, Fig. 1). The mean percentages of LD-1–LD-4 isoenzymes were not significantly different from baseline samples; however, LD-5 was significantly elevated on POD1 ($p < 0.025$). The mean postoperative LD-1:LD-2 ratios on POD1, POD2, and POD3 were not significantly different from preoperative values (Fig. 2). The mean values of the serum total CK and of the CK-MM isoenzyme were significantly elevated through POD3 ($p < 0.0005$). The mean value of CK-MB was

TABLE 1. The Values of Serum Isoenzyme LD in Patients Treated with Total Joint Arthroplasty

	Total LD (IU/l)	LD-1	LD-2	LD-3	LD-4	LD-5	LD-1:LD-2
THA patients							
Preop.	198 ± 23	18.5 ± 1.4	26.0 ± 1.1	20.9 ± 0.6	13.0 ± 0.6	21.0 ± 2.0	0.73 ± 0.04
POD1	227 ± 23	17.7 ± 1.8	23.4 ± 1.0	19.3 ± 0.8	13.4 ± 0.8	25.6 ± 1.5	0.77 ± 0.09
POD2	212 ± 30	20.3 ± 1.4	27.1 ± 1.1	19.9 ± 0.8	11.8 ± 0.7	21.6 ± 1.6	0.76 ± 0.06
POD3	187 ± 26	21.6 ± 1.2	28.0 ± 1.1	19.9 ± 0.6	11.3 ± 0.6	18.7 ± 1.4	0.77 ± 0.04
TKA patients							
Preop.	235 ± 37	21.6 ± 0.9	26.9 ± 1.1	19.7 ± 0.7	12.8 ± 0.7	18.9 ± 1.4	0.84 ± 0.05
POD1	336 ± 50	18.6 ± 1.2	25.0 ± 0.8	19.6 ± 0.6	13.6 ± 0.7	23.2 ± 1.3	0.75 ± 0.05
POD2	289 ± 52	18.3 ± 1.2	26.5 ± 1.3	19.4 ± 0.8	12.0 ± 0.6	23.7 ± 2.1	0.69 ± 0.03
POD3	251 ± 37	19.9 ± 1.2	28.3 ± 1.2	18.7 ± 0.9	12.6 ± 0.8	20.4 ± 1.4	0.73 ± 0.06

Values of isoenzymes are percentages ± SEM.

significantly elevated on POD1 ($p < 0.005$) and POD2 ($p < 0.05$), but not on POD3 (Fig. 3). The mean value of CK-BB was not significantly elevated on any of the three postoperative days. The mean percentages of CK-MM, CK-MB, and CK-BB were not significantly different on POD1-POD3. Eight of 75 postoperative samples (taken from six patients) had LD-1:LD-2 exceeding 1.0; however, none of these patients had absolute CK-MB values exceeding 18 IU/l. The maximum CK-MB value in any of the patients was 32 IU/l.

TOTAL KNEE ARTHROPLASTY

There were 27 preoperative and 81 postoperative samples. The mean serum total LD was significantly elevated on POD1 ($p < 0.001$) and POD2 ($p < 0.05$), but not on POD3 (Tables 1 and 2, Fig. 1). The mean percentages of LD-1-LD-4 isoenzymes were not significantly elevated; however, LD-5 was significantly elevated on POD1 ($p < 0.025$) and POD2 ($p < 0.01$). The mean LD-1:LD-2 never rose significantly and, in fact, was significantly lower on POD2 (p

TABLE 2. The Values of Serum Isoenzyme CK in Patients Treated with Total Joint Arthroplasty

	Absolute values (IU/l)				Percentages		
	TOTAL CK	CK-MM	CK-MB	CK-BB	CK-MM	CK-MB	CK-BB
THA patients							
Preop.	66 ± 8.4	63.5 ± 8.4	1.7 ± 0.5	0.8 ± 0.4	96.7 ± 1.0	1.9 ± 0.5	1.4 ± 0.5
POD1	427 ± 54.8	416.2 ± 54.6	7.8 ± 1.7	3.0 ± 2.6	97.4 ± 0.7	1.9 ± 0.4	0.7 ± 0.6
POD2	341 ± 48.2	333.6 ± 47.7	4.4 ± 1.3	3.0 ± 2.4	97.6 ± 1.2	1.5 ± 0.4	0.9 ± 0.9
POD3	220 ± 29.0	217.5 ± 28.8	1.8 ± 0.6	0.7 ± 0.5	98.9 ± 0.4	0.7 ± 0.2	0.4 ± 0.3
TKA patients							
Preop.	50 ± 4.7	48.1 ± 5.7	1.4 ± 0.4	0.5 ± 0.3	97.1 ± 1.1	2.0 ± 0.9	0.9 ± 0.5
POD1	125 ± 17.8	119.3 ± 17.6	4.6 ± 2.0	1.1 ± 0.6	95.7 ± 1.4	3.3 ± 1.3	1.0 ± 0.4
POD2	158 ± 25.4	153.9 ± 25.1	3.4 ± 1.1	0.7 ± 0.3	96.6 ± 1.3	2.6 ± 1.0	0.8 ± 0.5
POD3	101 ± 14.6	98 ± 14.6	2.0 ± 0.7	1.0 ± 0.6	96.5 ± 1.4	2.5 ± 1.3	1.0 ± 0.4

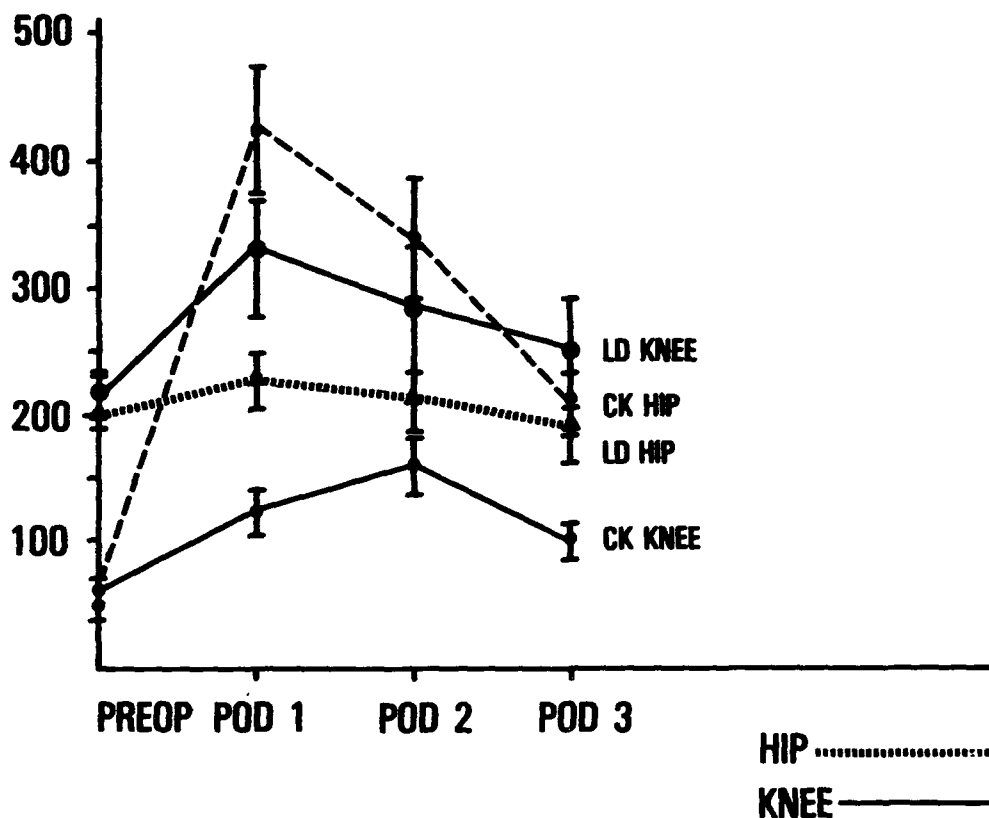


FIG. 1. The relationship of total CK and LD following total joint arthroplasty of the hip and knee.

< 0.005; Fig. 2). The mean absolute values of total serum CK and CK-MM were significantly elevated on POD1 ($p < 0.0005$), POD2 ($p < 0.0005$), and POD3 ($p < 0.005$). The mean value of CK-MB was significantly elevated on POD1 ($p < 0.05$), but not on POD2 or POD3 (Fig. 3). The mean absolute values of CK-BB were not significantly elevated on POD1-POD3. The mean percentages of CK-MM, CK-MB, and CK-BB were not significantly elevated on POD1-POD3. Six of 81 postoperative samples (five patients) had LD-1:LD-2 exceeding 1.0; however, none of these patients had CK-MB absolute values exceeding 13 IU/l. The maximum absolute CK-MB value was 52 IU/l. This patient did not experience any signs or symptoms of myocardial infarction and the postoperative electrocardiogram was un-

changed from the preoperative electrocardiogram. LD-1:LD-2 never exceeded 1.0 in this patient.

The elevations of total serum CK activity were significantly higher following total hip arthroplasty when compared to total knee arthroplasty on POD1 ($p < 0.0005$), POD2 ($p < 0.005$), and POD3 ($p < 0.0005$). Total mean LD elevation was significantly greater following total knee arthroplasty on POD1 ($p < 0.05$), but not on POD2 or POD3.

Three patients in this study group experienced postoperative chest pain and had electrocardiographic changes consistent with myocardial ischemia (electrocardiographic changes all resolved within 24 hours). Each patient had one sample with LD-1:LD-2 greater than 1.0; however, the maximum CK-MB value noted was only 13 IU/l.

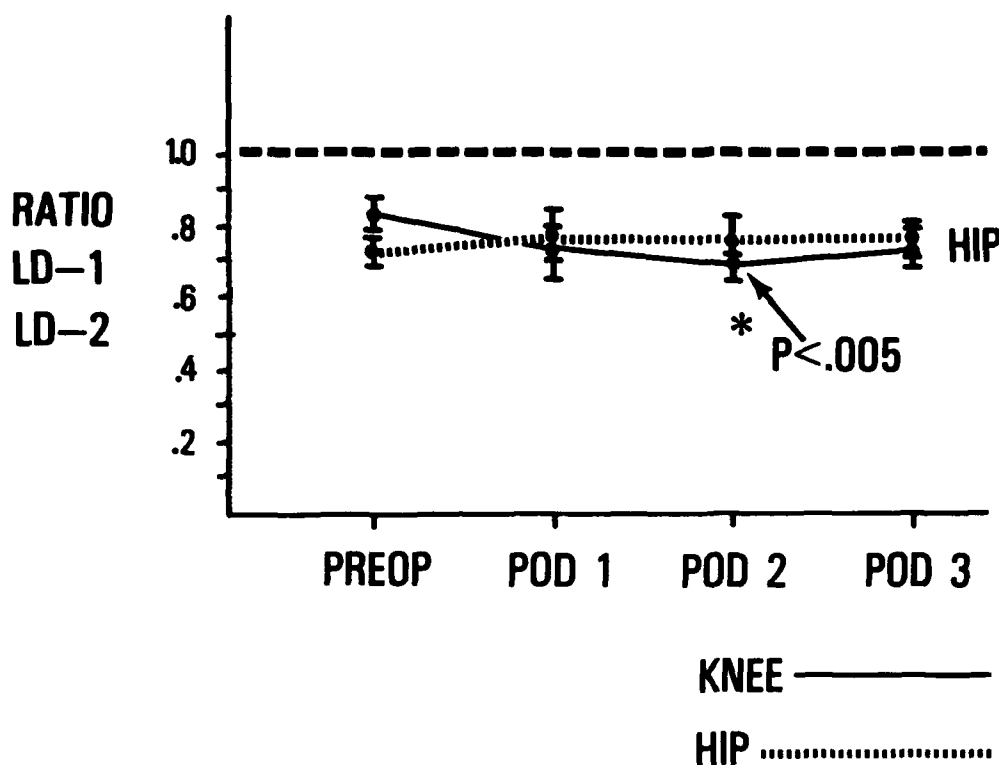


FIG. 2. LD-1:LD-2 following total joint arthroplasty of the hip and knee.

DISCUSSION

The diagnosis of acute myocardial infarction is made by history, physical examination, electrocardiographic changes, and determinations of serum enzymes.^{28,36} The history and physical examination are not specific for myocardial infarction since non-cardiac complications such as pulmonary embolism may accompany chest pain, dyspnea, and changes in vital signs.^{23,36} In addition, postoperative myocardial infarction can be painless in up to 50% of patients.⁷

Electrocardiograms, while specific in detecting transmural infarction, have been reported to be only 73% sensitive.²² A post-mortem study also reported that 30% of patients who had autopsy-proven myocardial infarctions had normal electrocardiograms.²⁰ Therefore, the diagnosis of postoperative myocardial infarction may depend on the

results of serum CK, LD, and isoenzyme determinations.

Creatine kinase is found primarily in skeletal muscle, myocardium, and brain, while smaller amounts can also be found in lung, bladder, and bowel. Three isoenzymes (CK-MM, CK-MB, and CK-BB) have been identified by electrophoresis. Skeletal muscle is comprised mainly of CK-MM, while myocardium is comprised of 25%–40% CK-MB.⁹ The CK-MB isoenzyme is virtually specific for myocardium. Galen^{8,9} reported that its presence in the serum is indicative of myocardial damage. Other studies have demonstrated that detectable amounts of CK-MB can be found in the serum of postoperative patients who have not experienced acute myocardial infarction.^{13,16,22} CK-BB can also be detected in the peripheral serum of postoperative patients.¹³

Lactate dehydrogenase is found in many

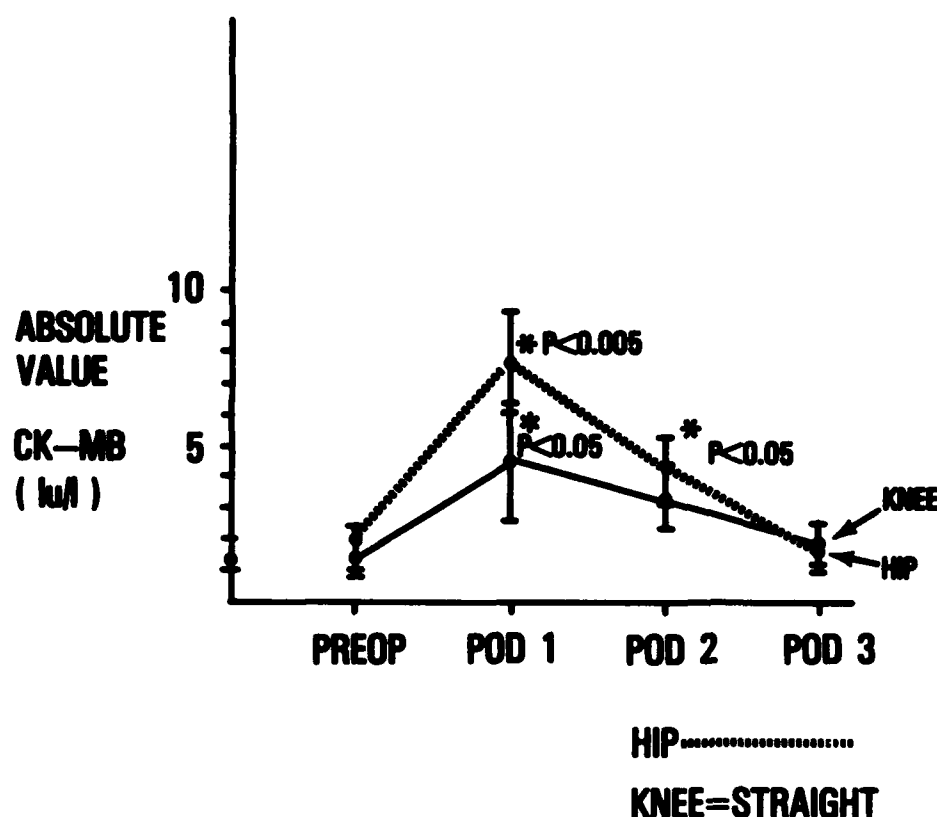


FIG. 3. The absolute values of myocardial-associated isoenzyme CK-MB following total joint arthroplasty of the hip and knee.

organs including myocardium, brain, kidney, lung, thyroid, bladder, uterus, bowel, spleen, liver, erythrocytes, and skeletal muscle.⁹ Five isoenzymes of LD have been identified by electrophoresis (LD-1-LD-5). The LD-1 isoenzyme comprises 40% of myocardial LD; however, LD-1 is not specific for myocardium since kidney, brain, and erythrocytes also have significant LD-1 activity.^{8,9} Skeletal muscle is comprised of 60% LD-5 and has virtually no LD-1 activity.^{8,9} In normal serum, LD-2 predominates and LD-1:LD-2 is less than 1.0.^{8,23}

Experimental and clinical studies have demonstrated that following acute myocardial infarction, total serum CK rises and the myocardial-associated isoenzyme, CK-MB, appears in the serum within six hours after the onset of symptoms.²³ Peak values are ob-

tained between 18 and 24 hours after infarction.^{9,13,23} In nonsurgical patients, CK-MB exceeding 5% of total serum CK is indicative of myocardial injury.^{9,23} LD-1 is also released into the serum following myocardial infarction resulting in LD-1:LD-2 greater than 1.0 (flipped LD pattern).^{9,13,23} The only other clinical situations that can result in a flipped LD pattern are hemolysis and renal infarction.⁸ Graeber¹³ found the sensitivity and specificity to be 99.9% in detecting myocardial infarction if two separate serum samples between 24 and 48 hours after surgery had both a flipped LD pattern and an absolute CK-MB value exceeding 50 IU/l. In postoperative patients, the absolute value of CK-MB may be a more reliable index of myocardial injury than the percentage of CK-MB for several reasons. First, a percent-

age does not indicate the amount of CK-MB present, *i.e.*, a CK-MB of 5% is quite different if the total CK activity is 1000 IU/l versus 100 IU/l. Second, the amount of CK-MB detected in the serum directly correlates with the amount of myocardial necrosis.²⁸ Finally, CK-MB fractions exceeding 5% of total CK activity have been documented in postoperative patients who did not experience myocardial infarction.¹⁶

The orthopedic literature contains few studies dealing with serum enzyme elevations in the postoperative period. Berglund and Bergstrom² found elevations of total CK and LD after hip surgery but did not study their isoenzymes.² Galen⁹ performed CK and LD determinations in nine patients treated with total hip arthroplasty and found elevations of total CK and LD, but isoenzyme analysis revealed that these elevations were due to skeletal muscle injury. Healey *et al.*¹⁶ demonstrated that CK-MB comprised 3%–8% of skeletal muscle CK activity when assaying paraspinal muscle biopsies for total CK and CK-MB activity. That study also demonstrated that 37% of patients treated with posterior spinal fusions had false positive elevations of CK-MB exceeding 5% of total CK activity. One patient in that study had a CK-MB absolute value of 369 IU/l ($4100 \text{ IU} \times 9\% \text{ CK-MB}$), but did not experience myocardial infarction.¹⁶

Skeletal muscle injury invariably occurs during total joint arthroplasty of the hip or knee from the necessary dissection and retraction. Consequently, it is easy to explain the elevations of LD-5 and CK-MM, which are the skeletal muscle isoenzymes of LD and CK, respectively. The present data indicate that greater than 95% of total serum CK elevation is due to CK-MM elevation; however, the absolute value of CK-MB did rise significantly following total joint arthroplasty of the hip or knee. These findings support the observation of Healey *et al.*¹⁶ that skeletal muscle contains small but significant amounts of CK-MB activity and that injury

to skeletal muscle can result in significant elevation of serum CK-MB. The maximal elevation of 52 IU/l of CK-MB occurred in a patient who did not manifest any other signs or symptoms suggestive of myocardial ischemia. It is also important to note that the percentages of CK-MM, CK-MB, and CK-BB did not change significantly. Similarly, LD-1:LD-2 did not rise significantly following total joint arthroplasty of the hip or knee.

The maximal rise in total serum CK was seven-fold following total hip arthroplasty and three-fold following total knee arthroplasty, while the rise in total LD was less than two-fold. Since CK-MM accounts for greater than 95% of total CK activity in muscle and LD-5 accounts for only 11% of total activity in muscle, it is apparent that skeletal muscle injury is reflected in total CK activity more so than total LD activity.⁹ Total hip arthroplasty resulted in significantly higher elevations of total CK than total knee arthroplasty (Fig. 4). The increased skeletal muscle dissection and retraction that occur during total hip arthroplasty compared to total knee arthroplasty probably account for this difference.¹⁸

It has been well documented that a circadian periodicity exists regarding the onset of symptoms or first elevations of CK-MB in nonsurgical patients who experience acute myocardial infarction.²⁵ The primary peak incidence of acute myocardial infarction occurs between 4 AM and 12 noon with a secondary peak incidence at 8 PM. This study, therefore, can be criticized for not determining serum enzyme values during the secondary peak incidence if the circadian periodicity applies to postoperative myocardial infarction. It would be expected, however, that the next morning's enzyme determinations (approximately ten hours later) would reveal elevations of serum CK-MB if myocardial infarction occurred during the secondary peak incidence. It is important to point out that all of the present postoperative

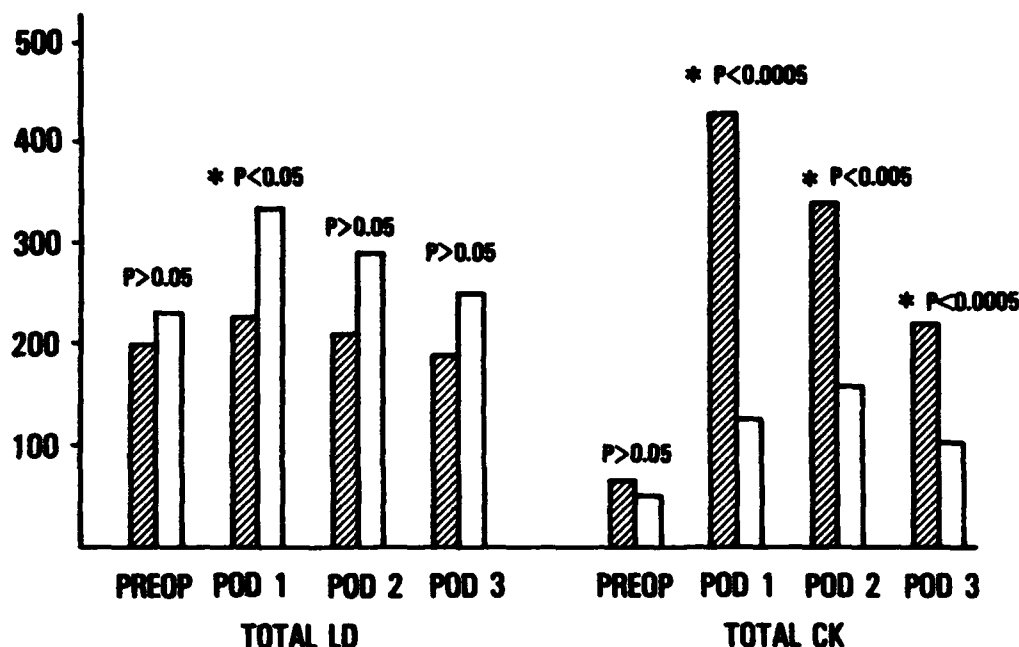


FIG. 4. A comparison of total CK and LD elevations between total hip arthroplasty (shaded area) and total knee arthroplasty (clear area).

enzyme values were obtained from patients during the primary peak incidence of myocardial infarction.

In summary, 45% of the patients in this study were at increased risk for perioperative myocardial infarction based on their age alone, *i.e.*, patients older than 70 years of age. These patients are representative of typical patients who are treated with total joint arthroplasty of the hip or knee.^{1,13} It is important, therefore, to define what effect the trauma of surgery has on these serum markers of myocardial injury if they are to be used in evaluating suspected postoperative myocardial infarction. Total joint arthroplasty of the hip or knee can result in significant elevations of serum CK-MB in patients who have not experienced postoperative myocardial infarction. The percentage of CK isoenzymes and LD-1:LD-2 do not rise significantly following total joint arthroplasty of the hip or knee. Detection of CK-MB in the serum following total joint arthroplasty

of the hip or knee, therefore, is not diagnostic of myocardial injury. Elevations of serum CK-MB exceeding 50 IU/l or 5% of total CK activity combined with LD-1:LD-2 greater than 1.0 should not be attributed to skeletal muscle injury alone.

ACKNOWLEDGMENTS

The authors would like to thank Linda G. Ellis and Susan Keenan for their technical assistance in the preparation of this manuscript.

REFERENCES

1. Becker, R. C., and Underwood, D. A.: Myocardial infarction in patients undergoing non-cardiac surgery. *Cleve. Clin. J. Med.* 54:25, 1987.
2. Berglund, B., and Bergstrom, K.: Serum enzymes after hip joint surgery. *Acta Orthop. Scand.* 50:671, 1979.
3. Borden, L. S., Heyne, T., Belhobek, G., Marks, K. E., Stulberg, B. N., and Wilde, A. H.: Total condylar prosthesis. *Orthop. Clin. North Am.* 13:123, 1982.
4. Callaghan, J. J., Salvati, E. A., Pellici, P. M., Wilson, P. D., and Ranawat, C. S.: Results of revision for mechanical failure after cemented total joint replacement, 1979 to 1982. *J. Bone Joint Surg.* 57A:1074, 1985.

5. Coventry, M. D., Beckenbaugh, R. D., Nolan, D. R., and Ilstrup, D. M.: 2012 total hip arthroplasties: A study of postoperative course and early complications. *J. Bone Joint Surg.* 56A:273, 1974.
6. Deburge, A., and GUEPAR: Guepar hinge prosthesis: Complications and results with two years' follow-up. *Clin. Orthop.* 120:47, 1976.
7. Dixon, W. J., and Massay, F. J.: *Introduction to Statistical Analysis*. New York, McGraw-Hill, 1969, pp. 119-138.
8. Galen, R. S.: The enzyme diagnosis of myocardial infarction. *Hum. Pathol.* 6:141, 1975.
9. Galen, R. S.: The enzyme diagnosis of myocardial infarction in the orthopaedic patient. *Orthop. Clin. North Am.* 10:451, 1979.
10. Gerber, S. D., and Harris, W. H.: Femoral head autografting to augment acetabular deficiency in patients requiring total hip replacement. *J. Bone Joint Surg.* 68A:1241, 1986.
11. Goldberg, V. M., and Henderson, B. T.: The Freeman-Swanson ICLH total knee arthroplasty. *J. Bone Joint Surg.* 62A:1338, 1980.
12. Goldman, L., Caldera, D. L., Nussbaum, S. R., Southwick, F. S., Krogstad, D., Murray, B., Burke, D. S., O'Malley, T. A., Gorolle, A. H., Caplan, C. H., Nolan, J., Carabello, B., and Slater, E. E.: Multifactorial index of cardiac risk in non-cardiac surgical procedures. *N. Engl. J. Med.* 297:845, 1977.
13. Graeber, G. M.: Creatine kinase: Its use in the evaluation of perioperative myocardial infarction. *Surg. Clin. North Am.* 65:539, 1985.
14. Graeber, G. M., Synder, R. J., Zajchuk, R., and Brott, W. H.: A comparison of serum isoenzyme levels of creatine phosphokinase and lactic dehydrogenase in patients undergoing thoracic operations and patients admitted to a coronary care unit. *Ann. Thorac. Surg.* 30:364, 1980.
15. Hamilton, H. W., and Joyce, M.: Long-term results of low-friction arthroplasty performed in a community hospital, including a radiologic review. *Clin. Orthop.* 211:55, 1986.
16. Healey, J. H., Kagen, L. J., Velis, K. P., and Levine, D. B.: Creatine kinase MB in skeletal muscle and serum of spine-fusion patients. *Clin. Orthop.* 195:282, 1985.
17. Hess, J. W., MacDonald, R. P., and Nathow, G. J. W.: Serum creatine phosphokinase: Evaluation of a commercial spectrophotometric method. *Clin. Chem.* 13:994, 1967.
18. Hoppenfield, S., and deBoer, P.: *Surgical Exposures in Orthopaedics: The Anatomic Approach*. Philadelphia, J.B. Lippincott, 1984, pp. 316-394.
19. Hori, R. Y., Lewis, J. L., Zimmerman, J. R., and Compere, C. L.: The number of total joint replacements in the United States. *Clin. Orthop.* 132:46, 1978.
20. Johnson, W. J., Achor, R. W. P., Burchell, H. B., and Edwards, J. E.: Unrecognized myocardial infarction. *Arch. Intern. Med.* 103:253, 1959.
21. Kavanaugh, B. F., Ilstrup, D. M., and Fitzgerald, R. H.: Revision total hip arthroplasty. *J. Bone Joint Surg.* 67A:517, 1985.
22. Kornberg, A.: Reversible enzymatic synthesis of diphosphopyridine nucleotide in organic phosphate. *J. Biol. Chem.* 182:779, 1950.
23. Lott, J. A., and Stang, J. M.: Serum enzymes and isoenzymes in the diagnosis and differential diagnosis of myocardial ischemia and necrosis. *Clin. Chem.* 26:1241, 1980.
24. Lovelack, J. E., Griffiths, H. J., Silverstein, A. M., and Anson, P. S.: Complications of total knee replacement. *AJR* 142:985, 1984.
25. Muller, J. E., Stone, P. H., Turi, Z. G., Rutherford, J. D., Czeisler, C. A., Parker, C., Poole, W. K., Passamani, E., Roberts, R., Robertson, T., Sobel, B. E., Willerson, J. T., Braunwald, E., and the Milis Study Group: Circadian variation in the frequency of onset of acute myocardial infarction. *N. Engl. J. Med.* 313:1315, 1985.
26. Nielson, L., and Ludwigsen, B. J.: Improved method for determination of creatine kinase. *J. Lab. Clin. Med.* 62:159, 1963.
27. Oliver, I. T.: Spectrophotometric method for the determination of creatine phosphokinase and myokinase. *Biochem. J.* 61:116, 1955.
28. Petersdorf, K. G., Adams, R. D., Braunwald, E., Isselbacher, K. J., Martin, J. B., and Wilson, J. D.: *Harrison's Principles of Internal Medicine*. New York, McGraw-Hill, 1983, p. 1433.
29. Ranawat, C. S., Atkinson, R. E., Salvati, E. A., and Wilson, P. D.: Conventional total hip arthroplasty for degenerative joint disease in patients between the ages of forty and sixty years. *J. Bone Joint Surg.* 66A:751, 1984.
30. Rosalki, S. B.: An improved procedure for serum creatine phosphokinase determination. *J. Lab. Clin. Med.* 69:696, 1967.
31. Salvati, E. A., Wilson, P. D., Jolley, M. N., Vakili, F., Aglietti, P., and Brown, G. C.: A ten year follow up study of our first one hundred consecutive Charnley total hip replacements. *J. Bone Joint Surg.* 63A:753, 1981.
32. Shindell, R., Neuman, R., Connally, J. F., and Jordan, O. M.: Evaluation of the Noiles hinged knee prosthesis. *J. Bone Joint Surg.* 68A:579, 1986.
33. Soudry, M., Binazzi, R., Insall, J. N., Nordstrom, T. J., Pellici, P. M., and Goulet, J. A.: Successive bilateral total knee replacement. *J. Bone Joint Surg.* 67A:573, 1985.
34. Thomas, B. J., Salvati, E. A., and Small, R. D.: The CAD hip arthroplasty. *J. Bone Joint Surg.* 68A:640, 1986.
35. Wilkinson, J., and Steciw, B.: Evaluation of a new procedure for measuring serum creatine kinase activity. *Clin. Chem.* 16:370, 1970.
36. Wyngaarten, J. B., and Smith, L. H.: *Cecil's Textbook of Medicine*. Philadelphia, W. B. Saunders, 1985, pp. 288-295.